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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
01/26/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,121	THOMAS, MARIAN	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,24 and 29-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,24 and 29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/15/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The prosecution of this application has been transferred from examiner Joseph Kudla to examiner Isis Ghali

The receipt is acknowledged of applicant' amendment and IDS both filed 09/15/2008.

Claims 1-14, 16-23 and 25-28 have been canceled and claims 29-33 have been added.

Claims 15, 24, and 29-33 are pending and included in the prosecution.

The following new grounds of rejections have are necessitated by applicant's amendment:

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claim 15, 24, 29-33 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11-13 and 20 of U.S. Patent Application 10/564191 (Monteith et al.), in view of all Staniforth et al. (WO 2001/078694 and cited by Applicant) and Muller-Walz et al. (WO 02/078671 and cited by Applicant (citations from English language equivalent of US Non-provisional Application 10/473874 and provided to Applicant)). Although the conflicting claims are not identical, they are not patentably distinct from each other because Monteith et al. teach a method of inhibiting chemical degradation of the same active substance in a formulation comprising a carrier, an active ingredient substance and a functional equivalent of the calcium stearate found in the instant invention.

Monteith et al. does not teach the use calcium stearate to aid in minimizing chemical degradation.

Staniforth et al. teach a secondary amine containing active ingredient (i.e., formoterol) that is used in a formulation with magnesium stearate and lactose (page 43, lines 16-19) for an inhalation device (reference claim 1). But Staniforth et al. also teaches the additive material can include salts of stearic acid (page 17, lines 16-23) and

specifically calcium stearate (page 35, line 30 and page 40, Table 4). Staniforth et al. teach that the additive material limits the interaction of the active ingredient and the carrier molecule by occupying all of the high energy sites on the carrier particle allowing for easier release of the active from the carrier in the lungs (page 13, lines 12-21).

Muller-Walz et al. teach a medical suspension aerosol formulation and the use of certain salts as excipients in such formulation (page 1, lines 3-5). Muller-Walz et al. teach the salt is a carboxylic acid salt and includes such stearate salts such as magnesium and calcium stearate (page 6, lines 32-35). These salts have the ability to improve suspension stability and chemical stability (page 7, lines 4-10). The salts are found to improve chemical stability through improved moisture resistance (page 10, line 10-14).

It would have been obvious to one of ordinary skill in the art at the time of the invention that, in view of Staniforth et al, and Muller-Walz et al., the magnesium and calcium stearate salts are functional equivalents and an obvious variant of the instant invention unless unexpected results can be shown, therefore instant claims are rendered obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

3. The examiner acknowledges applicant's request to defer this provisional rejection until either this application or application '191 is found allowable. However, "provisional"

double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only remaining rejection in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other applicant into a double patenting rejection at the time the one application issues as a patent. MPEP § 804, subsection I.B.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 32 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the active ingredients of claim 32 or salts of said active ingredients does not reasonably provide enablement for a solvate of an active ingredient of claim 32. The specification does not provide sufficient guidance nor does it enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a

disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are: 1. the nature of the invention, 2. the state of the prior art, 3. the predictability or lack thereof in the art, 4. the amount of direction or guidance present, 5. the presence or absence of working examples, 6. the breadth of the claims, 7. the quantity of experimentation needed, and 8. the level of the skill in the art.

In the instant case:

The nature of the invention: The nature of the invention is an active ingredient of claim 32, or a salt of said active ingredient. There is no teaching of solvates of the active ingredients of claim 1 in the specification.

The state of the prior art and predictability or lack thereof in the art: It is the state of the prior art that the term "solvate" found in the claims is defined as a compound formed by solvation (the combination of solvent molecules with molecules or ions of the solute. It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation

of solvates or hydrates and hence generalizations cannot be made for a series of related compounds (See Vippagunta, et al.).

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active in vivo. Solvates and hydrates cannot always be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular hydrate or solvate.

The amount of direction or guidance present and the presence or absence of working examples: There is no direction or guidance present in the specification or working examples present in the specification are that defines or relates to what solvates are being included in the elected invention.

The breadth of the claims: The breadth of the claims is a conjugate of claim 32 or a pharmaceutically acceptable salt or solvate thereof.

The quantity of experimentation needed and the level of the skill in the art: While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to prepare compounds with various solvents without any direction as to what compounds form solvates with which solvents. Without a showing or guidance as to how to make solvates of an active ingredient of claim 32 it would require undue experimentation to

figure out the solvents, temperatures and reaction times that would provide solvates of the above compounds.

To overcome this rejection, Applicant should submit an amendment deleting the term "solvates."

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 15, 24, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Almarsson et al. (US Patent US 6,559,293), in view of all Staniforth et al. (WO 2001/078694 and cited by Applicant), Muller-Walz et al. (WO 02/078671 and cited by Applicant (citations from English language equivalent of US Non-provisional Application 10/473874 and provided to Applicant)) and Keller et al. (WO 00/28979 and cited by Applicant (citations from English language equivalent of US Patent 6,645,466)).

The instant claims are drawn to a method of inhibiting chemical degradation of primary and secondary amine containing active ingredients with a formulation that contains as a carrier lactose and calcium stearate. The active ingredients are those recited by claim 32.

Almarsson et al. teach that "The suitability of a particular excipient may also depend on the specific active ingredients in the dosage form. For example, the decomposition of some active ingredients can be accelerated by some excipients such as lactose, or when exposed to water. Actives ingredients that comprise primary and secondary amines are particularly susceptible to such accelerated decomposition" (column 17, lines 15-21).

Almarsson et al. does not teach a method of formulation where the addition of calcium stearate can inhibit the chemical degradation of a primary and secondary amine containing active ingredient.

Staniforth et al. teach a secondary amine containing active ingredient (i.e., formoterol) that is used in a formulation with magnesium stearate and lactose (page 43, lines 16-19) for an inhalation device (reference claim 1). Staniforth et al. teaches the carrier is lactose (reference claim 4) and the additive material includes salts of stearic acid (page 17, lines 16-23) and specifically 0.2% calcium stearate (page 35, line 30 and page 40, Table 4). Staniforth et al. teach that the additive material limits the interaction of the active ingredient and the carrier molecule by occupying all of the high energy sites on the carrier particle allowing for easier release of the active from the carrier in the lungs (page 13, lines 12-21).

Muller-Walz et al. teach a medical suspension aerosol formulation and to the use of certain salts as excipients in such formulation (page 1, lines 3-5). Muller-Walz et al. teach the salt is a carboxylic acid salt, such as calcium stearate (page 6, lines 32-35) and has the ability to improve suspension stability and chemical stability (page 7, lines

4-10). The salts are found to improve chemical stability through improved moisture resistance (page 10, line 10-14).

Keller et al. teach the improvement of moisture resistance of dry powder formulations (column 1, lines 8-10) with magnesium stearate (column 4, lines 44-45). Keller et al. teach a dry powder formulation where lactose and magnesium stearate are mixed then combined with a secondary amine containing active ingredient (i.e., formoterol) (column 9, Example 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention that because it was known that compounds that comprise primary and secondary amines are particularly susceptible to such accelerated decomposition especially when brought into contact with some excipients such as lactose or when exposed to water as taught by Almarsson et al., any agent which minimized interaction between a primary and secondary amine containing compound formulated with lactose or provided moisture resistance would protect the primary and secondary amine containing compound from chemical degradation. One of ordinary skill in the art would have been apprised of Staniforth et al., Muller-Walz et al., Keller et al. and realized that the stearates (such as calcium and magnesium) would have provided protection against moisture and limited interaction between the lactose and active ingredient. Therefore, combining the references of Almarsson et al., in view of all Staniforth et al., Muller-Walz et al. and Keller et al. provides the suggestion that moisture exposure and chemical interaction needs to me minimized and motivation to utilize a stearate, such as calcium stearate, to do so, thus rendering instant claims 15, 24, 29 and 30 obvious.

Response to Arguments

8. Applicant's arguments filed 09/15/2008 have been fully considered but they are not persuasive.

Applicant argues that Almarsson identifies the problem solved by the instant invention and recognizes that the suitability of particular excipients may depend on the specific active ingredients in a dosage form. Almarsson provides a general teaching that lactose or water may have a detrimental effect on active ingredients. Almarsson provides no teaching or suggestion that degradation of an active ingredient in the presence of lactose, can be ameliorated by use of calcium stearate. Almarsson teaches away from the use of calcium stearate by specifically referring to antioxidants to reduce the rate by which an active ingredient will decompose.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Almarsson is relied upon to show that at the time of the invention, the problem that applicant was trying to solve was already known and manipulated by others. Almarsson recognized the problem of accelerated decomposition of some compounds when brought into contact with some excipients such as lactose or when exposed to water, Almarsson further realized that any agent which minimized interaction between compounds susceptible to decomposition with lactose or provided moisture resistance

would protect this compound from chemical degradation. The protection of compounds from moisture resistance and consequently protection against their degradation using stearate is taught by references combined with Almarsson. The reference does not teach away from the present invention. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." In re Gurley, 27 F.3d 551,553 (Fed. Cir. 1994). Reading Almarsson's reference does not lead to direction divergent from the path taken by applicant because the reference desired to prevent decomposition of active agent when combined with lactose in one composition and one having ordinary skill in the art would seek solving this problem by adding compounds that protect from moisture and consequently protect from degradation

Applicant argues that Staniforth is concerned with formulations for inhalation to the lung and with the use of additive materials to promote the release of active ingredient particles from carrier particles. Staniforth speaks generally of a wide range of potential additive materials. The reference expresses a particular preference for amino acid additive materials (page 16 lines 17-18), but also mentions (Example 12) that calcium stearate may be used. While Staniforth suggests that an additive material limits

the interaction of the active ingredient and the carrier molecule by occupying all of the high energy sites on the carrier particle, there is nothing in the Staniforth reference to suggest that any of the additive materials would have the effect of inhibiting chemical degradation of an active ingredient or to single out calcium stearate from the laundry list of other additive materials listed in the reference.

In response to these arguments, it is argued that one of ordinary skill in the art would have been apprised of Staniforth et al., and realized that the stearates (such as calcium and magnesium) would have provided protection against moisture and limited interaction between the lactose and active ingredient because Staniforth et al. teach that the additive material limits the interaction of the active ingredient and the carrier molecule by occupying all of the high energy sites on the carrier particle allowing for easier release of the active from the carrier in the lungs. Further, Staniforth et al. teaches calcium stearate as preferred additive because it is exemplified by the reference, and it is not picked from laundry list. Although the reference listed various additives, however, preferred calcium stearate. Limitation of interaction disclosed by the reference reads on improving stability and inhibiting degradation.

Applicants argue that Muller-Walz relates to the use of various salts, including calcium stearate to improve aerosol suspension stability, the mechanical function of the dosing valve, the dosing precision, and the chemical stability of an active substance suspended in hydrofluoroalkane propellant. Muller-Walz is non-analogous to the instant application since, the principal problem addressed by the reference is stability of the

aerosol suspension, not the stability of the active ingredient itself. The reference does mention that salts "can also improve the chemical stability of the pharmaceutical active compound, in particular the moisture resistance of moisture-sensitive active compounds.", but the comment is made in the context of aerosol formulations and does not address interactions with carriers such as lactose. In contrast to the aerosol formulation of Muller-Walz in which moisture is thought to cause degradation of an active compound, the present application relates to formulations in which degradation of active ingredient substances is caused, by interaction with a carrier, such as lactose.

In response to applicant's argument that “problem addressed by the reference is stability of the aerosol suspension, not the stability of the active ingredient itself”, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In response to applicant's argument that Muller-Walz reference is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant’s endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Muller-Walz reference is in the field of applicant’s endeavor as it is directed to pharmaceutical formulation, and in particular aerosol formulation, and further the reference is reasonably pertinent to the particular problem with which the applicant was concerned which is stability of aerosol formulation using

calcium stearate. Therefore, Muller-Walz reference is an analogous art. The reference teaches stabilizing active agent by calcium stearate, which is suggestion of inhibition or protection against degradation. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Applicant argues that Keller is directed to improvement of moisture resistance of dry powder formulations. Keller relates to the influence of moisture on the fine particle during the storage of an inhalation powder. Keller provides no teaching with regard to chemical degradation of an active compound, much less the use of calcium stearate to prevent such degradation.

In repose to this argument, it is argued that Keller et al. suggest that moisture exposure and storage instability need to be minimized and suggest utilizing stearate,

such as calcium stearate. It is further argued that the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Magnesium and calcium stearate salts are functional equivalents as disclosed by the combination of the references.

Applicant further argues that the references provided disjointed teachings regarding physical interactions of active ingredients and lactose, moisture resistance, and aerosol suspension stability. The references, alone or in combination, simply fail to teach or suggest Applicant's claimed method of inhibiting chemical degradation of an active ingredient substance. Despite the failure of the references to teach or suggest the invention, the Office maintains that the invention is obvious. In order to make the obviousness rejection, the Office asserts that "any agent which minimized interaction between a primary and secondary amine containing compound formulated with lactose or provided moisture resistance would protect the primary and secondary amine containing compound from chemical degradation.". The correlation of minimized interaction, or moisture resistance, with inhibition of chemical degradation is unsupported by the references, and such assertion is improper without adequate support. Applicant requests that support be provided for the Office's assertion.

In response to these arguments, it is argued that it is well established that the claims are given the broadest interpretation during examination. A conclusion of

obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). The combination of the cited prior art would have suggested the present invention as a whole. The combination would have provided formulation comprising active agent, lactose carrier and calcium stearate and it is expected that the composition is stable against degradation because compounds and their properties are inseparable. The burden is on applicants to show that the claimed process resulted in novel and unobvious difference between the claimed product and prior art product since the Patent Office does not have the facilities for preparing the claimed materials and comparing them with the prior art inventions. See *In re Best*, 562 F.2 1252, 195 USPQ 430 (CCPA 1977); and *In re Fitzgerald et al.*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980). It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design

community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL. (2007).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have prima facie been obvious within the meaning of 35 U.S.C. 103 (a).

9. Claims 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Almarsson et al., Staniforth et al., Muller-Walz et al., Keller et al. and further in view of Roche et al. (WO 03/088943 provided by applicant).

The combined teachings of Almarsson et al., Staniforth et al., Muller-Walz et al., and Keller et al. are previously discussed as set forth in this office action.

Although the combination of the references teach drugs in the form of dry powders provided in inhalers, however, the references do not explicitly teach the active agents claimed by claim 32.

Roche et al. teach a dry powder pharmaceutical inhaler composition (Abstract). Roche et al. teach the pharmaceutically active agent can be any therapeutic molecule in dry powder form that is suitable to be administered by inhalation (p. 4, lines 6-8). Roche et al. teach preferred active agent is 3-(4-{[6- ({(2R)-2-hydroxy-2-[4-hydroxy-3-

(hydroxymethyl)phenyl]ethyl}amino)hexyl] oxy}butyl) benzenesulfonamide (p. 5, lines 25-30; reference claim 14), which is the substance of instant claims 32, and the agent can be present in a concentration of 0.01% - 99% of the total weight of the composition (instant claim 31) (p. 6, lines 22-24). Roche et al. further disclose the composition contains lactose (p. 2, claim 11).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide formulation stable against degradation and suitable for inhaler comprising active agent, lactose and calcium stearate as taught by the combination of Almarsson et al., Staniforth et al., Muller-Walz et al., Keller et al., and replace the active agent with 3-(4-{[6- ({(2R)-2-hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl}amino)hexyl] oxy}butyl) benzenesulfonamide disclosed by Roche et al. One would have been motivated to do so because Roche et al. teach that this compound is preferred compound for delivery by inhaler in combination with lactose. One would have reasonably expected formulating composition for inhaler comprising3-(4-{[6- ({(2R)-2-hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl}amino)hexyl] oxy}butyl) benzenesulfonamide, lactose and calcium stearate wherein the composition is stable against degradation in the inhaler.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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